REMARKS

Claims 1-19 were pending in the present application. Claims 1-3, 7-10 and 15-19 were rejected. Claims 1-6, 11-13, and 16-18 are herein amended. Claims 7-10 and 19 are herein cancelled without prejudice. New claims 20-22 are added herein. No new matter has been added.

Applicants' Response to Objections to the Sequence Listing

The Office Action states that the text of the specification is not in compliance with the requirements for Sequence Identifiers because multiple, different sequences are referred to as SEQ ID NO. 1. Specifically, the specification refers to the general formula sequence and the specific sequences (10-3L, 10-4F, 10-3F, and 10-3A) as SEQ ID NO. 1. In order to correct this issue, Applicants herein amend the specification to refer to sequence 10-3L as SEQ ID NO. 2, sequence 10-4F as SEQ ID NO. 3, sequence 10-3F as SEQ ID NO. 4 and sequence 10-3A as SEQ ID NO. 5. The general formula retains the identifier of SEQ ID NO. 1. Applicants herewith amend the claims accordingly, and herewith submit a Second Substitute Sequence Listing. No new matter has been added.

Currently Withdrawn Claims

Applicants herein amend withdrawn claims 4-6 and 11-13 in order improve their clarity and form, and to be consistent with the claims under currently under examination, in the event

that the withdrawn claims are rejoined or a divisional application is filed directed at these claims. Additionally, Applicants herein add new claims 20-22.

Applicants' Response to Objections to the Specification

The Office Action states that the specification filed on May 11, 2007 was objected to because it fails to indicate what part of the specification was amended or modified. It appears that a marked-up version of the specification was intended to be submitted along with the clean version of the Substitute Specification on May 11, 2007, but was inadvertently omitted. Both a marked-up and clean version of the Substitute Specification were previously filed on December 20, 2006. Applicants direct the Examiner's attention to the changes made on pages 7, 11, 12 and 15 of the Substitute Specification filed on December 20, 2006. Additionally, it is noted that the Substitute Specification (clean) submitted on May 11, 2007 was identical to the Substitute Specification (clean and marked-up) submitted on December 20, 2006.

Applicants herewith submit a Second Substitute Specification. This Second Substitute Specification corrects four errors. First, the Second Substitute Specification provides for the suggested section headings. Second, the Second Substitute Specification revises the SEQ ID NOs in order to be consistent with the Substitute Sequence Listing, discussed above.

Furthermore, the Second Substitute Specification replaces the symbols "□" and "■" with the text "white bars" and "black bars," respectively, in the Brief Description of the Drawings, since these symbols may not appear properly when printed.

Additionally, Applicants herein amend the specification in order to clarify the claimed subject matter. Specifically, Applicants amend the recitations of "14 to 23 residues of amyloid β-peptide" to "the 14th to 23rd residues of amyloid β-peptide." Applicants also submit a Substitute Abstract, which corrects a similar error in the Abstract.

Finally, since the Examiner noted difficulty in distinguishing words individually due to the text formatting, Applicants note that the Second Substitute Specification uses the "Times New Roman" font instead of the "Courier" font. Thus, Applicants submit that this improves readability. However, it is noted that this has altered the pagination somewhat. No new matter has been added. Both clean and marked-up versions of this Second Substitute Specification and Substitute Abstract are herewith submitted. Applicants respectfully submit that the Second Substitute Specification and Substitute Abstract fully comply with all U.S.P.T.O. requirements. Favorable reconsideration is respectfully requested.

Applicants' Response to Claim Rejections under 35 U.S.C. §101

Claims 1-3, 7-10 and 15-19 were rejected under 35 U.S.C. §101 as failing to comply with the utility requirement.

It is the position of the Office Action that the claimed subject matter lacks a specific and substantial asserted utility or a well-established utility. Specifically, the Office Action states that the specification lacks a disclosure of a specific biological significance of the claimed peptide. The Office Action acknowledges that the specification discloses that the claimed peptides form aggregates with Aβ(10-35) *in vitro*. However, the Office Action states that the specification does

not teach "the relevance between finding the enhanced aggregation of Aβ(10-35) by the claimed peptide and diagnosis of Alzheimer's disease." The Office Action states that the use of the claimed peptides to amplify amyloid fibrils would actually result in a more serious pathological condition. Further, the Office Action states that the specification lacks disclosure of the use of the peptides to diagnose Alzheimer's.

In response, Applicants first note that the amplification of the amyliod fibrils is performed *ex vivo*. Thus, the amplification does not result in a more serious pathological condition in the patient. It was well known in the art that plasma contains Aβ(1-40) and Aβ(1-42). See Mehta et al., attached hereto. The reagent of the present invention makes it possible to amplify and measure a minute amount of Aβ contained in plasma.

The causal relationship between Aβ in plasma and Alzheimer's disease was recently verified by Schupf N et al, attached hereto. It is an important technology to provide for accurate measuring of Aβ contained in plasma. By using the claimed reagents, sensitivity of measurement improves due to the amplification of a minute amount of Aβ in plasma. A reagent or peptide which is used for accurate diagnosis of Alzheimer's disease has a well-established utility, since such a diagnosis helps with, for example, medical and family planning. Therefore, for at least the above reasons, Applicants respectfully submit that the claimed embodiments fully comply with the utility requirement of 35 U.S.C. §101. Favorable reconsideration is respectfully requested.

Applicants' Response to Claim Rejections under 35 U.S.C. §112

Claims 1-3 and 7-10 were rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is the position of the Office Action that claims 1-3 and 7-10 are indefinite because they recite "14 to 23 residues of amyloid-b-peptide" without a reference to a precise amino acid sequence represented by a SEQ ID NO.

In response, Applicants herein amend the claims in order to clarify their subject matter. In particular, Applicants herein amend claim 1 to recite that the peptide has the general formula represented by SEQ ID NO. 1. Further, Applicants herein amend claims 2 and 3 to recite that the peptide is the specific peptide of SEQ ID NO. 2 and SEQ ID NO. 3, respectively. These peptides are also referred to in the specification as 10-3L and 10-4F, respectively. Additionally, Applicants herein add new claim 20, which recites that the peptide is the specific peptide of SEQ ID NO. 4. This peptide is also referred to in the specification as 10-3F. Applicants herein cancel claims 7-10 without prejudice.

Additionally, Applicants respectfully note that the disclosure of "14 to 23 residues of amyloid-b-peptide" does not refer to the quantity of residues. Rather, this is a mistranslation, and should refer to the "14^{th} to 23^{rd} residues of amyloid-b-peptide." The full sequences of Aβ(1-40) and Aβ(1-42) were well known in the art, as illustrated by Thorsett et al. and Findeis et al., both of which are attached thereto. Therefore, it would have been obvious to one having ordinary skill

in the art that the claimed peptide is a modification of the 14th to 23rd residues of the wildtype Aβ peptide. Favorable reconsideration is respectfully requested.

Claims 1-3, 7-10 and 15-19 were rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement.

It is the position of the Office Action that while the specification is enabling for artificial peptides 10-3F, 10-4F and 10-3L, it is not enabling for undefined peptides derived from Aβ (14-23) or undefined peptides derived from 14-23 residues of amyloid β-protein with any substitutions as claimed.

In response, Applicants herein amend the independent claims to recite the general formula represented by SEQ ID NO. 1. Additionally, Applicants herein amend the independent claims to recite Leu-Leu, Leu-Phe, and Phe-Leu as possible amino acids for the "X-Y" positions. Applicants also amend the dependent claims to recite the specific peptides of SEQ ID NO. 2, SEQ ID NO. 3, and add dependent claims to recite SEQ ID NO. 4. These are the 10-3F, 10-4F and 10-3L peptides, respectively, which are regarded as being enabled. Accordingly, Applicants respectfully submit that all pending claims are enabled. Favorable reconsideration is respectfully requested.

Applicants' Response to Claim Rejections under 35 U.S.C. §102

Claims 1 and 7 were rejected under 35 U.S.C. §102(b) as being anticipated by Tjernberg et al. (J. Biol. Chem. 1999. 274: 12619-12615).

It is the position of the Office Action that Tjernberg discloses the embodiments as claimed. The Office Action states that Tjernberg teaches a reagent including "Aβ(14-23), which meets the limitation of a peptide consisting of 14-23 residues of amyloid-β-peptide as recited in instant claims 1 and 7 (see p. 12622, 2nd column, 2nd paragraph)." September 16, 2008 Office Action, page 15, lines 5-8. It appears that the Office Action regards Tjernberg as disclosing the wildtype sequence of Aβ(14-23) on page 12622. However, this is inaccurate. On page 12622, Tjernberg discloses a peptide having the sequence of Ala-Gln-Lys-Leu-Val-Phe-Phe-Ala-Glu-Ala. This is not the wildtype sequence of Aβ(14-23). However, the wildtype sequence of Aβ(13-23) is in fact disclosed by Tjernberg at page 12261, column 2.

In response, Applicants respectfully note that amended claim 1 does not recite the wildtype sequence of Aβ(14-23). Rather, claim 1 recites only modifications to the wildtype sequence. Tjernberg does not disclose any of the recited modifications. Therefore, Applicants respectfully submit that Tjernberg does not disclose or suggest the peptide as recited by the pending claims. Favorable reconsideration is respectfully requested.

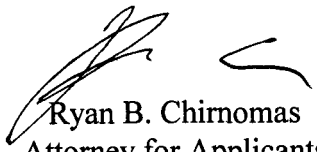
For at least the foregoing reasons, the claimed invention distinguishes over the cited art and defines patentable subject matter. Favorable reconsideration is earnestly solicited.

Should the Examiner deem that any further action by applicants would be desirable to place the application in condition for allowance, the Examiner is encouraged to telephone applicants' undersigned attorney.

If this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. The fees for such an extension or any other fees that may be due with respect to this paper may be charged to Deposit Account No. 50-2866.

Respectfully submitted,

WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP



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Enclosures:
Second Substitute Specification (clean)
Second Substitute Specification (marked-up)
Substitute Abstract (clean)
Substitute Abstract (marked-up)
Submission of Second Substitute Sequence Listing
Second Substitute Sequence Listing (electronic)
Second Substitute Sequence Listing (paper)
Thorsett ED et al., "Therapeutic approaches to Alzheimer's disease." *Current Opinion in Chemical Biology*, 2000, 4: 377-382.
Findeis MA et al., "Modified-Peptide Inhibitors of Amyloid β-Peptide Polymerization." *Biochemistry*, 1999, 38: 6791-6800.
Mehta PD et al., "Amyloid β protein 1-40 and 1-42 levels in matched cerebrospinal fluid and plasma from patients with Alzheimer's disease." *Neuroscience Letters*, 2001, 304: 102-106.
Schupf, N et al., "Peripheral Aβ subspecies as risk biomarkers of Alzheimer's disease." *Proceedings of the National Academy of Sciences*, September 16, 2008, vol. 105, no. 37, pp. 14052-14057.